A PHARMACOVIGILANCE STUDY OF IDENTIFICATION AND REPORTING OF DRUG INTERACTION IN MEDICAL WARD IN CK BIRLA HOSPITALS [RBH] JAIPUR"

A Synopsis
Submitted in partial fulfillment
For the award of

Ph.D.

In

Pharmacy

PHARMACOLOGY

JULY 2021

Supervised By: - Submitted by:-
Dr. Naveen SinghalRamanand Sharma

LIST OF TABLES

SR.NO	CONTENT	PAGE NO.
1	INTRODUCTON	3-8
2	REVIEW OF LITERATURE	9-12
3	AIM AND OBJECTIVES	13
4	WORK PROCESS	14
5	MATTERIAL AND METHODS	15
6	REFERENCES	16-17
7	ANNEXURE	18-20

INTRODUCTON

1.1 Drug Interaction

- A Drug interaction is an interaction between a drug and some other substance, such as another drug or a certain type of food, which prevents the drug from working correctly.
- An interaction can either increase or decrease the effectiveness and/or the side effects of a drug.
- Interaction play a role in patient who use drugs which may interact with biologicals.[1]

1.2 Causes of Drug Interaction

- People who are taking multiple medications for extended periods of times.
- Patients with renal or hepatic impairments because their metabolism and excretion will be impaired.
- Determining who will experience an interaction is largely unpredictable because various factors (age, lifestyle, diet, underlying disease) of an individual can affect the likeness that the drug will interact.[2]

1.3 Types Drug Interactions

- Typically interactions between drugs come to mind (drug-drug interaction). However, interactions may also exist between drugs and foods (drug- food interactions), as well as drugs and medicinal plants or herbs (drug-plant-interactions) and also (drug-disease interactions) But there are essentially two types of drug interactions
- Pharmacodynamics
- Pharmacokinetic

Pharmacodynamic

- Pharmacodynamic interactions are those in which the effect of one drug is changed by the presence of another drug action at the same biochemical or molecular site (e.g., drug receptor or second messanger system) on the same target organ, or one a different target but one that is associated with a common physiological process essentially when one drug modulates the pharmacologic effect of another by producing additive, synergistic or antagonistic effects.

Additive Effect

- Am effect in which two substances or actions used in Combination produce total effect the same as the sum of the individual effects.

Synergistic effect

- Interaction between two or more drug agent, entities, factors, or substances the produces an effect greater than the sum of their individual effects.

Antagonistic effect

- Interaction of two or more drug substances such that the action of any one of them on living cells or tissues is lessened or diminished.

Pharmacokinetics

Pharmacokinetic interactions are those in which one drug results in an alteration (increase or decrease) of the concentration of another drug in the system. Different parameters can be affected by pharmacokinetic interactions, including a drug's bioavailability, volume of distribution, peak level, clearance and half life. Such changes can lead to changes in drug plasma concentrations and ultimately increase of the risk of side effects or diminish the effects or diminish the efficacy of one or more drugs. Pharmacokinetic interactions are more complicated and difficult to predict because of the interaction drugs often have unrelated actions.

Drug-Drug Interactions

Drug- drug interaction occur when a drug interacts, or interferes, with another durg. This can alter the way one of both of the drugs act in the body, or cause unexpected side effects.

1. Aspinin+ Warfarin Synergism (excessive bleeding)
2. Antibiotic+ Blood Thinner Antagonism (Less effect.)

Drug Food interactions

A drug food intraction happens when the food you eat effects the ingredients in a medicine you are taking so the medicine cannot work the way it should

1. Bisphosphonates+ Any drug Reduced effectiveness of drug
2. Acetaminophen+ Alcohol Liver damage

Drug- Disease interactins

Drug condition interaction occur when a drug worsens or exacerbates an existing medical condition

1. Nasal decongestants+ Hypertension Increased blood pressure
2. NSAID'S + Asthmatic Patients Air way Obstruction

1.3 Preventing Measures of Drug Interaction

- Avoiding combination therapy
- Dose adjustment of main drug
- Adjusting the time of intake of two drugs
- Monitoring of combination therapy when used
- Educating the patient on potential interactions is essential
- Advanced screening techniques need to used to identify interactions

1.4 Mechanisms by Which Drug Interactions Occur

- When there is an increase or decrease in:
- The absorption of a drug into the body

- Distribution of the drug in the body
- Changes made to the drug through the body's metabolism
- Elimination of the drug from the body
- When one drug alters the concentration of a substance that normally occurs in the body thus reducing or enhancing the desired effects of another drug[3].

1.5 Consequences

- Drug Interactions can:
- Reduce the desired effects of a drug
- Increase the adverse effects of a drug
- Result in unnecessary pain and suffering
- Increase the beneficial effects of a drug
- Decrease the adverse effects of a drug[4]

1.6 Top 10 Drug Interactions

- Warfarin ~ Sulfa Drugs
- Warfarin ~ Macrolides
- Warfarin ~ Quinolones
- Warfarin ~ Phenytoin
- ACE Inhibitors ~ Potassium Supplements
- ACE Inhibitors ~ Spironolactone
- Digoxin ~ Amiodarone
- Digoxin ~ Verapamil
- Theophylline ~ Quinolones
- Warfarin ~NSAIDs

WAYS OF PREVENTING DRUG INTERACTIONS

- A list of all medications that they are currently taking or have used in the last few weeks (3~4) to the healthcare providers. This list should include over-the-counter medications, vitamins, food supplements, and herbal remedies.
- Keep the list of medications current and inform healthcare providers when any drug is added or discontinued.
- Report any changes in lifestyle to healthcare providers (i.e. diet, exercise).
- Ask healthcare providers about any possible drug interaction that may occur with a medication. Work with healthcare personnel to eliminate any unnecessary medications

  Pay attention and record time of day when medications are taken.

- Be aware, be comfortable, and be actively involved in the treatment/drug therapy process.[13]

WHERE TO FIND MORE INFORMATION:

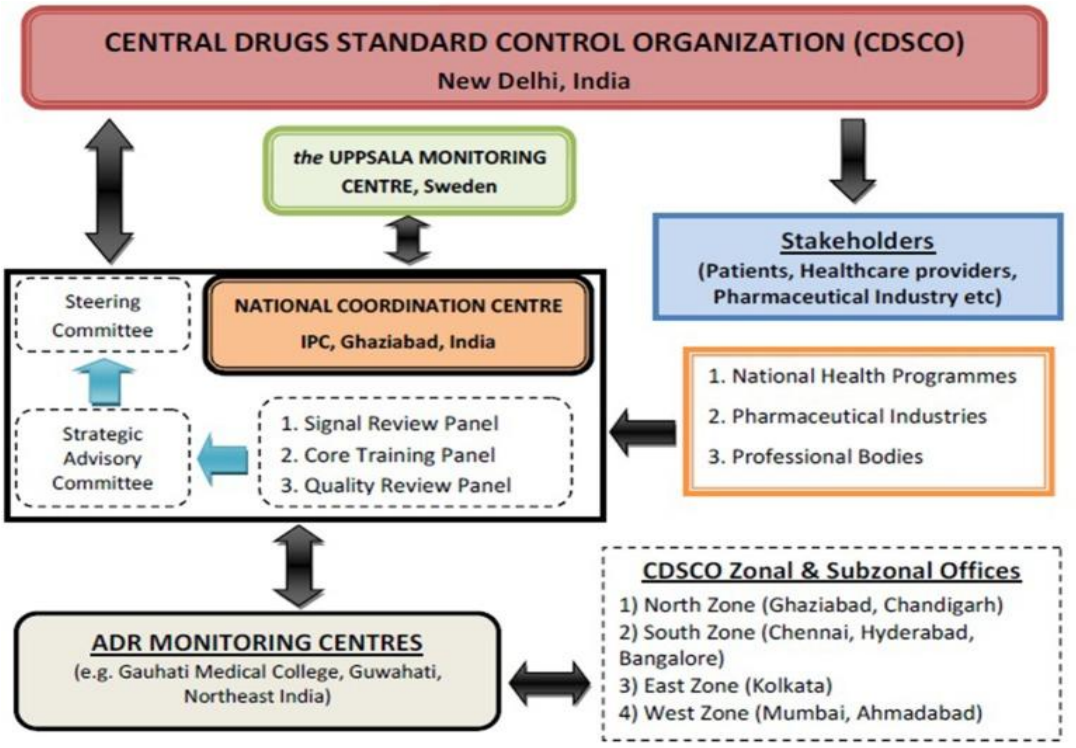
- Talk to a healthcare provider (ask the doctor about the prescribed medications).
- Talk to a pharmacist.
- Read the information that accompanies the medication.
- Research at a local library or on the internet with reliable and valid sources (i.e. drugs.com).[14]

PHARMACOVIGILANCE

- Pharmacovigilance (PV) is defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem. WHO established its Programme for International Drug Monitoring in response to the thalidomide disaster detected in 1961. Together with the WHO Collaborating Centre for International Drug Monitoring, Uppsala, WHO

promotes PV at the country level. At the end of 2010, 134 countries were part of the WHO PV Programme. The aims of PV are to enhance patient care and patient safety in relation to the use of medicines; and to support public health programmes by providing reliable, balanced information for the effective assessment of the risk-benefit profile of medicines.

- Drug safety and pharmacovigilance remains a dynamic clinical and scientific discipline.it play a vital role in ensuring that doctors, together with the patient, have enough information to make a dicision when it comes to choosing a drug for treatment.[15]


CENTRAL DRUGS STANDARD CONTROL ORGANIZATION (CDSCO)
New Delhi, India
the UPPSALA MONITORING CENTRE, Sweden
Stakeholders
(Patients, Healthcare providers, Pharmaceutical Industry etc)
Steering Committee
NATIONAL COORDINATION CENTRE
IPC, Ghaziabad, India
Strategic Advisory Committee
1. Signal Review Panel
2. Core Training Panel
3. Quality Review Panel
1. National Health Programmes
2. Pharmaceutical Industries
3. Professional Bodies
ADR MONITORING CENTRES
(e.g. Gauhati Medical College, Guwahati, Northeast India)
CDSCO Zonal & Subzonal Offices
1) North Zone (Ghaziabad, Chandigarh)
2) South Zone (Chennai, Hyderabad, Bangalore)
3) East Zone (Kolkata)
4) West Zone (Mumbai, Ahmadabad)

REVIEW OF LITRATURE

1. Khamis, Doran; El Mouden,2018Chakrabartishaon and michorfranziska "pharmacokinetics and drug interactions determine optimum combination strategies in computational models of cancer evolution", the identification of optimal drug administration schedules to battle the emergence of resistance is a major challenge in cancer research. The existence of a multitude of resistance mechanisms necessitates administering drugs in combination, significantly complicating the endeavor of predicting the evolutionary dynamics of cancers and optimal intervention strategies. A thorough understanding of the important determinants of cancer evolution under combination therapies is therefore crucial for correctly predicted treatment outcomes. Here we developed the first computational strategy to explore pharmacokinetic and drug interaction effects in evolutionary models of cancer progression, a crucial step towards making clinically relevant predictions. We found that incorporating these phenomena into our multiscale stochastic modeling framework significantly changes the optimum drug administration schedules identified, often predicting nonintuitive strategies for combination therapie
2. Murtazaghulamet al.2015 "assessment of potential drug drug interaction and its associated factors in the hospitalized cardiac patient" drug drug interaction may result in the alteration of therapeutic response.

   Hospitalized cardiac patients need more attention regarding drug–drug interactions due to complexity of their disease and therapeutic regimen. This research was performed to find out types, prevalence and association between various predictors of potential drug–drug interactions (pDDIs) in the Department of Cardiology and to report common interactions. This study was performed in the hospitalized cardiac patients at Ayub Teaching Hospital, Abbottabad, Pakistan. Patient charts of 2342 patients were assessed for pDDIs using Micromedex® Drug Information. Logistic

regression was applied to find predictors of pDDIs. The main outcome measure in the study was the association of the potential drug–drug interactions with various factors such as age, gender, polypharmacy, and hospital stay of the patients.

3. Singh H, dulhani n[1], "A Pharmacovigilance study in medicine department of tertiary care hospital in Chhattisgarh ,india" ADR monitoring and reporting help in detected and prevented of reoccurrence of ADRs.

   A prospective, observational evaluation of the ADRs conducted over a period of 6 months in Department of Medicine in Government Medical College, Jagdalpur. During the study period, a total of about 4850 patients visited the OPD and inpatient ward of medicine department, and 154 ADRs events were reported. Out of 154 reports that were identified, a higher percentage of ADRs in females (51.29%) was observed as compared to males (48.7%). Of the 154 ADRs, 76 (49.35%) were found to be mild, 55 moderate (35.71%), and 23 severe (14.93%). A total of 99 (64.28%) ADRs were observed in patients receiving four or more medications concurrently. Conversely 55 (35.71%) ADRs were detected in patients using three or less medicines. The largest number of reports was associated with antimicrobial therapy (28.57%), followed by antihypertensive (24.02%) and antidiabetics (14.28%). Among the affected organ systems, gastrointestinal ADRs constituted a major component (39.61%) followed by skin reactions (28.57%). On causality assessment, nearly 36.36% ADRs were considered as probable, 31.16% possible, and 9.74% could not be categorized and were placed under unassessable. Expected, limited ADR are permissible in normal clinical setting, but the present study focuses on the result showing increased and amplified ADR associated with the polypharmacy practices, which may be curtailed with rational drug prescribing habit.

4. Sharma Himanshu et al 2007 “A Pharmacovigilance study in the department of medicine of a university teaching hospital” the aim of the present study was to monitor advers drug reactions in the medicine out patient department.

   Method A prospective evaluation of the ADRs reported in the Department of Medicine of our University Teaching Hospital over a period of 4-months was conducted. Results During the study period, a total of 600 patients visited the Medicine OPD and 122 ADRs were reported. Out of 122 reports that were identified, a higher percentage of ADRs in males (52.4%) was observed as compared to females (47.5%). Of the 122 ADRs, 50 were found to be mild (41.0%), 49 moderate (40.2%), and 23 severe (18.2%). A total of 71 (58.0%) ADRs were observed in patients receiving 4 or more medications concurrently. Conversely 46 (37.7%) ADRs were detected in patients using 3 or less medicines. The largest number of reports were associated with antihypertensive therapy (39.3%), followed by antimicrobials (31.1%) and antidiabetics (10.7%). Amongst the organ systems affected, gastrointestinal ADRs constituted a major component (24.7%) followed by skin reactions (22.2%). On causality assessment, nearly 29.5% ADRs were considered as probable, 33.6% possible and 6.6% could not be categorised and were placed under unassessable. Conclusion The present work is the maiden pharmacovigilance study conducted at our university teaching hospital. The data presented here will be useful in future, long term and more extensive ADR monitoring in the hospital and in promotion of rational prescribing and drug use in the hospital.

5. ‘RijkomjeannetleE.F.zwart-van’ et_al.2009 “frequency and nature of drug-drug interaction in a dutch university hospital” drug-drug interaction may led to often preventable adverse drug events and health damage.

   Especially within hospitals, this might be an important factor, as patients are severely ill and multiple medications was prescribed simultaneously. The objective of this

study was to measure the frequency and nature of DDI alerts in a Dutch university hospital.

All patients hospitalized in the University Medical Centre Utrecht in 2006 who were prescribed at least one medication were included. The frequency of DDIs was calculated as: (i) the percentage of patients experiencing at least one DDI, and (ii) the percentage of prescriptions generating a DDI alert. Based on the national professional guideline, DDIs were classified into categories of potential clinical outcome, management advice, clinical relevance (A–F) and available evidence (0–4).

6. ‘Rc kumara swamy’, ramanijignesh u.et al.2014 “prevalence of polypharmacy and drug to drug interaction in a teriary care teaching hospital” inappropriate prescription and using of multiple medication can lead to morbidity and mortality.

   Especially within hospitals, this might be an important factor, as patients are severely ill and multiple medications may be prescribed simultaneously. The objective of this study was to measure the frequency and nature of DDI alerts in a Dutch university hospital.

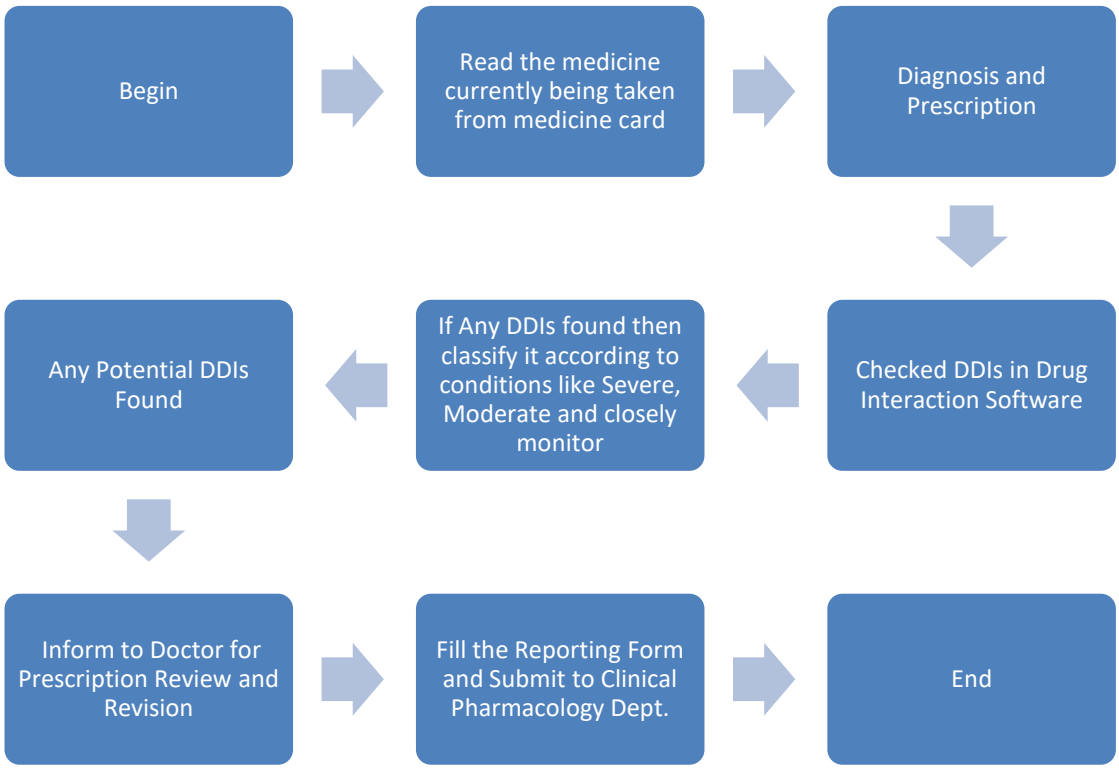
   All patients hospitalized in the University Medical Centre Utrecht in 2006 who were prescribed at least one medication were included. The frequency of DDIs was calculated as: (i) the percentage of patients experiencing at least one DDI, and (ii) the percentage of prescriptions generating a DDI alert. Based on the national professional guideline, DDIs were classified into categories of potential clinical outcome, management advice, clinical relevance (A–F) and available evidence (0–4).

AIM AND OBJECTIVES

- To improve patient care and safety in relation to the use of medicines, and all medical and paramedical interventions
- To improve public health and safety in relation to the use of medicines
- To improve patient compliance and to provide responsible self-medication.

WORK PROCESS

Flow Chart


Begin
Read the medicine currently being taken from medicine card
Diagnosis and Prescription
Checked DDIs in Drug Interaction Software
If Any DDIs found then classify it according to conditions like Severe, Moderate and closely monitor
Any Potential DDIs Found
Inform to Doctor for Prescription Review and Revision
Fill the Reporting Form and Submit to Clinical Pharmacology Dept.
End

MATTERIAL AND METHODS

- The prospective observation prescription analysis study for drug-drug interaction. .
- This study was including hospital in-patients treated in medicine department for various diseases.
- Drug Interaction observed in the study were entered in database with following information:
- Age/Sex
- Types of interaction
- Diagnosis

The **Medscape/Drugs.com drug interaction checker software** was used to identify **DRUG- DRUG INTERACTION.**

REFERENCES

1. Trumic E, Pranjic N, Begic L, Bečić F. Prevalence of Polypharmacy and Drug Interaction Among Hospitalized Patients: Opportunities and Responsibilities in Pharmaceutical Care. Materia Socio-Medica. 2012;24(2):68–72.

2. .Harugeri A, Joseph J, Parthasarathi G, Ramesh M, Guido S. Potentially inappropriate medication use in elderly patients: a study of prevalence and predictors in two teaching hospitals. J Postgrad Med. 2010;56(3):186–91.

3. Biswas P, Biswas A. Setting standards for proactive pharmacovigilance in India: The way forward. Indian J Pharmacol. 2007, 75-92.

4. Gosney M, Tallis R. Prescription of contraindicated and interacting drugs in elderly patients admitted to hospital. Lancet. 1984;2(8402):564–67.

5. Rothberg MB, Pekow PS, Liu F, Korc-Grodzicki B, Brennan MJ, Bellantonio S, et al. Potentially inappropriate medication use in hospitalized elders. J Hosp Med. 2008;3(2):91–102.

6. Lared NL. Pharmacists' role in reporting adverse drug reactions in an international perspective. 2003: 107-115.

7. Veena DR, Padma L, Patil S. Drug prescribing pattern in elderly patients in a teaching Hospital. Journal of Dental and Medical Sciences. 2012;1(5):39–42.

8. Olsson S. The role of the WHO Programme for International Drug Monitoring in coordinating worldwide drug safety efforts. 2003:48-56.

9. WHO. The Importance of Pharmacovigilance, Safety Monitoring of medicinal products. World Health Organization 2002: 33-35.

10. Report E. Effective communications in Pharmacovigilance. International Conference on Developing Effective Communications in Pharmacovigilance, Erice, Sicily 1997; 24-27.

11. Shuka SS, Gidwani B, Pandey R, Rao SP, Singh V,.Importance of Pharmacovigilance in Indian Pharmaceutical Industry. Asian J. Res. Pharm. Sci. 2012: 4-8.

12. Hornbuckle K, Wu H-H, Fung MC. 1999. Evaluation of spontaneous adverse event reports by primary reporter - a 15-year review (1983 to 1997). Drug Info. 33, 1117-24.

13. Egberts GPG, Smulderes M, De Konig FHP, et al. 1996. Can adverse drug reactions be detected earlier: a comparison of reports by patients and professionals.2005: 78-96

14. Norwood PK, Sampson AR. A statistical methodology for postmarketing surveillance of adverse drug reaction reports. 1988: 45-58.

15. Fialová D, Topinková E, Gambassi G, et al. Potentially Inappropriate Medication Use Among Elderly Home Care Patients in Europe. JAMA. 2005;293(11):1348–58.

ANNEXURE

ANNEXURE 2.

Case Report Form:-

CASE REPORT FORM	DRUG INTERACTION REPORTING FORM

1. PARTICULARS OF PATIENT

Patient Name..... **Age /Gender**...../.....

M.R.N NO.....**Department**..... **DOA**.....

2. PATHOPHYSIOLOGY.....

.....

.....

.....

.....

.....

3. TYPE OF INTERACTION.....

.....

4 .NAME OF SUSPECTED DRUG-DRUG/DRUG FOOD.....

.....

5. SIGNS AND SYMPTOMS.....

.....

6 .REPORTERS NAME

SIGNATURE.....

DATE.....

7 .DR SIGNATURE.....

ANNEXURE 3.

Patients Informed Consent:-

INFORMED CONSENT FORM

Patient name:

MRN No:

- Title of the Project: A Pharmacovigilance Study and Reporting of Drug Interaction in Tertiary care Hospital
- Name of the Principal Investigator Mr. Mukesh Kumar Sharma (Head of Department of Research and Academics), C K Birla Hospitals (RBH), Jaipur
- I,.....son/ daughter/ wife of ..... consent to be a subject of the proposed study.
- I have received the information sheet on the above study and have read and / or understood the written information.
- I consent to take part in the study and I am aware that my participation is voluntary.
- I understand that I may withdraw at any time without this affecting my future care. I understand that the information collected about me from my participation in this research and sections of any of my medical notes may be looked at by responsible persons (ethics committee members / regulatory authorities). I give access to these individuals to have access to my records.
- I have been informed well enough about the examination and tests to be conducted during this study.
- I understand I will receive a copy of the patient information sheet and the informed consent form.
- I am consenting to the study by my own will without any pressure or force whatsoever after understanding everything.
- Therefore, I will be myself responsible for any harm, untoward effects or benefits whatsoever due to the study and I will not make any claim afterwards.